STUDIES WITH AN ACTIVE PROSTHETIC MYOCARDIUM

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Many experimental and clinical studies of surgical excision of the acute myocardial infarct have demonstrated improvement of ventricular function[1-4]. Since an infarcted area acts as a focus of electrical irritability and frequently exhibits paradoxical systolic expansion quite similar to that observed in chronic ventricular aneurysm, excision of the infarct can be beneficial[5]. Infarctectomy has been particularly successful when it involved no more than 7-15%[1,3] of the left ventricular wall. However, there is general agreement that removal and resection of large areas of the left ventricle diminish left ventricular volume to such an extent that failure results[1-7]. Even when ventricular volume is maintained by inserting a patch of synthetic material, after acute resection, loss of viable muscle leads to a reduction in cardiac output[8]. After extensive excision, it therefore appears necessary not only to maintain ventricular volume, but also to replace myocardial function. Toward this objective we have designed a prosthetic myocardium which can be implanted in the left ventricle and pneumatically driven to restore function to that area. Hemodynamic results in 13 acute studies in dogs are described in this report.

MATERIALS AND METHODS

Adult mongrel dogs weighing from 26 to 32 Kg were used in the studies. The animal was anesthetized with pentobarbital sodium (25 mg/Kg), given intravenously. A cuffed endotracheal tube was inserted, and the animal was ventilated through a volume controlled respirator* with 100% oxygen, at the rate of 20 respirations/min, and a tidal volume of 600 to 800 cc. The chest was opened in a median sternotomy and the heart was supported in a pericardial cradle. After heparinization (3 mg/Kg) the animal was prepared for cardiopulmonary bypass. A 16 gauge Bardic arterial perfusion cannula was inserted into the right femoral artery. The superior and inferior venae cavae were cannulated with a No. 40 Fr cardiac catheter through 2 separate atriotomies. The pump-oxygenator consisted of a roller pump+, and a bubble oxygenator#. The entire circuit was primed with lactated Ringer's solution and blood. Catheters were positioned to measure aortic and left ventricular pressures. Aortic flow was recorded with an electromagnetic flow probe& placed in the supracoronary position.

After total cardiopulmonary bypass was instituted and the heart fibrillated electrically, a portion of the anterior left ventricular wall, approximately 5 cm in diameter, was excised. A 5.5 cm diameter, circular dacron velour patch, coated on its outer surface with a medical grade silicone adhesive° to secure hemostasis, was placed over the defect. The patch was attached to the endocardial surface of the left ventricle with interrupted sutures that passed through a strip of dacron felt, thereby providing reinforcement to the wound edge. Sixteen additional evenly spaced activating sutures were fastened to the rim of the patch, gathered in a tube (Figure 1) and connected to the piston of a pneumatic acuator. A control unit, synchronized to the cardiac cycle by the electrocardiogram, provided a pneumatic drive to the actuator (Figure 2). At the beginning of systole, vacuum in the cylinder caused the piston to exert tension on the sutures and draw the wound edge together. At the end of systole, positive pressure on the piston released tension on the sutures allowing the wound edge to expand in phase with ventricular dilation (Figure 3).

After implantation of the prosthesis, cardiopulmonary bypass was terminated. At this stage of the experiment, all dogs were in profound cardiogenic shock, with a peak aortic systolic pressure of less than 80 mm Hg. The prosthetic myocardium was then activated until the monitored hemodynamic parameters stabilized, and then turned off. Following stabilization, the device was turned on and off for intervals of approximately 2 to 5 mins to observe the changes in hemodynamic function produced by intermittent assistance. Care was taken to provide accurate synchronization of the prosthetic myocardium to the cardiac rhythm in order to maximize hemodynamic support. Periods of observation averaged 2 hrs.

In each dog, recordings were analyzed for 5 Off-On transitions (activation) and 5 On-Off transitions (arrest). Determinations of left ventricular systolic pressure, left ventricular end-diastolic pressure, aortic systolic pressure, and cardiac output were made in 4 heart cycles immediately preceding and following each transition.

At the end of each experiment, the heart and excised section of the left ventricle were weighed. The percent of the excised left ventricle was then estimated, taking the weight of the intact free left ventricular wall as

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*Metomatic veterinary anesthesia machine, Ohio Medical Products, Ferndale, Michigan.
+Modular Roller Pump, Sarns, Inc., Ann Arbor, Michigan.
#Temptrol Q-100, Bentley Laboratories, Irvine, California.
&Biotronex Laboratory, Silver Spring, Maryland.
°Silastic Medical Grade Adhesive, Dow Corning, Midland, Michigan.

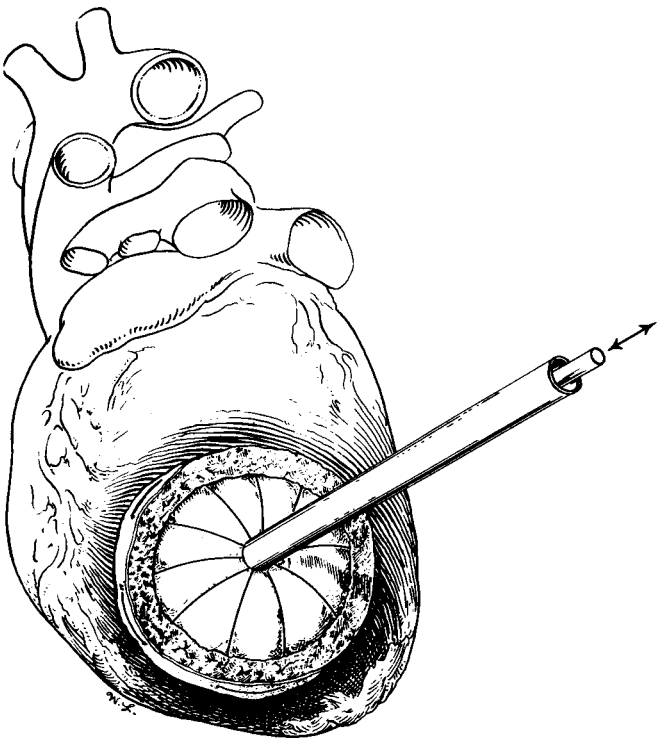

Figure 1. The prosthetic myocardium implanted in the left ventricular wall. Activating sutures are attached to the wound edge and are gathered in a tube at the center of the prosthesis.

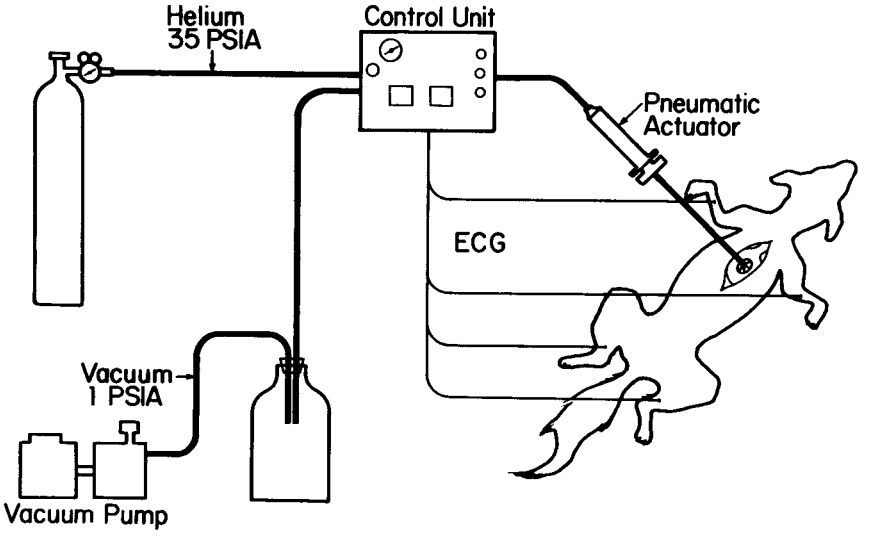

Figure 2. Experimental set-up showing pneumatic actuator and control unit for the prosthetic myocardium.

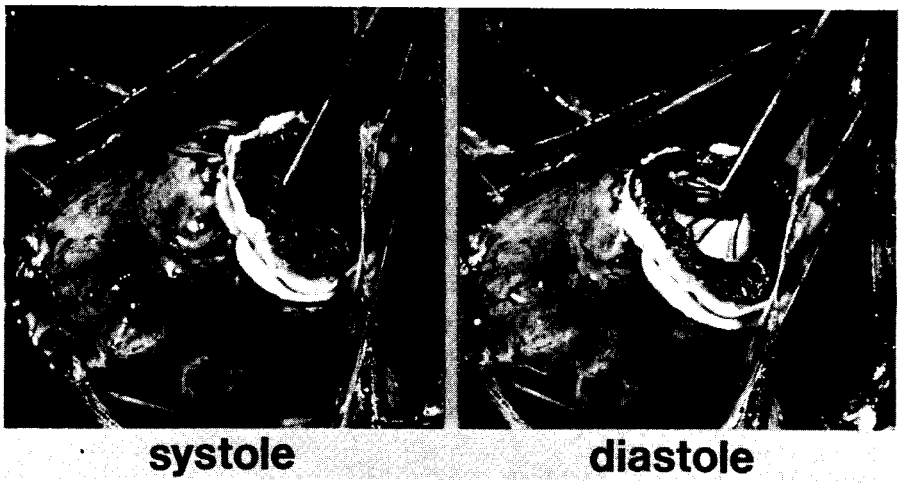

Figure 3. The activated implanted prosthetic myocardium, in systole (left) and diastole (right).

TABLE I

CHANGE IN HEMODYNAMIC PARAMETERS AFTER ACTIVATION (OFF-ON) AND ARREST (ON-OFF) OF THE PROSTHETIC MYOCARDIUM

Exp. No.	Dog Weight (Kg)	% L.V. Free Wall Excised	Aortic Systolic Pressure % Change		L.V. Systolic Pressure % Change		L.V. End-Diastolic Pressure % Change		Cardiac Output (ml/min/Kg) % Change	
			Off-On	On-Off	Off-On	On-Off	Off-On	On-Off	Off-On	On-Off
27	28.0	24.5	3.8	6.8	7.1	- 0.9	8.3	5.5	8.7	15.2
29	26.0	23.1	11.3	13.6	7.6	11.4	17.5	10.4	19.6	22.2
31	32.0	17.6	12.7	15.4	10.4	12.3	11.3	3.9	21.3	42.7
32	28.0	31.5	8.0	10.6	9.1	9.6	15.9	26.0	16.8	18.5
34	26.0	22.1	2.1	9.5	0.8	9.3	9.3	23.9	12.9	17.2
35	27.0	25.6	7.2	9.7	6.4	10.4	4.9	6.1	28.7	26.2
36	30.0	30.1	5.5	7.3	6.0	6.9	27.2	25.6	15.5	15.4
37	27.0	28.1	7.6	3.5	7.4	4.2	27.8	28.1	13.1	16.7
38	27.0	24.9	9.4	19.3	17.2	22.3	24.4	22.4	32.8	42.0
39	30.0	25.2	9.8	12.8	8.3	12.7	20.4	13.9	27.5	40.6
41	28.0	27.7	17.3	16.3	18.6	15.8	7.7	22.6	12.2	19.0
42	26.0	28.6	9.4	12.7	9.9	15.7	31.5	16.1	17.1	64.4
43	28.0	32.4	14.2	10.3	15.1	10.1	12.4	12.0	40.5	35.0
Mean	27.8	26.3	9.1	11.4	9.5	10.8	16.8	16.6	20.5	28.8
S.D.	1.8	4.1	4.2	4.3	4.1	5.5	8.8	8.6	9.3	15.0
Combined Mean %			10.3		9.8		16.5		24.0	
S.D.			3.9		4.8		7.3		10.0	

39% of the total heart weight[9]. In addition to determining hemodynamic changes, a cinecardioangiographic study of one dog was conducted to observe ventricular volume and mitral valve function during activation of the implanted prosthesis.

RESULTS

A total of 43 dogs were employed in this study. The first 26 dogs were used to evolve the surgical technique and to develop the prosthesis and the actuating mechanism. A series of 17 experiments was then conducted for evaluation of hemodynamic parameters with an activated prosthesis. Three dogs died of air embolism during cardiopulmonary bypass and one dog died of shock. Data for the remaining 13 dogs are presented in Table I.

Throughout the studies, the actuating sutures remained firmly attached despite a total tension of 49 newtons on the device. There was no leakage around the edge of the wound and no seepage through the dacron material. Although one-third of the papillary muscle was removed when the defect was created, implantation of the patch appeared to fix the muscle adequately and restored ventricular function. Improvement in left ventricular emptying following activation of the prosthesis can be seen by comparing 2 ventriculograms. Figure 4 shows the left ventricle in systole and diastole with the device inactive. Figure 5 represents the same view with the device activated. Note that in Figure 4 only the hi-anterior and a small area of the posterior wall contracted during systole. There was no movement at the apex where the prosthesis was implanted. When the prosthesis was activated, however, the anterior, posterior, and apical walls of the ventricle contracted during systole (Figure 5), resulting in a marked improvement in ejection fraction. In the dog studied, there was evidence of mitral regurgitation.

Hemodynamic response to the activation of the prosthetic myocardium is presented for one dog in Figure 6. Peak left ventricular systolic pressure, averaged over 4 cycles before and after applying force on the sutures, increased from 71 mm Hg to 96 mm Hg, aortic systolic pressure increased from 71 mm Hg to 92 mm Hg, left ventricular end-diastolic pressure decreased from 12 mm Hg to 11 mm Hg, and cardiac output increased from 1.4 L/min to 2.4 L/min. Such changes in hemodynamic parameters, averaged over 5 instances of activation and arrest by measuring 4 cycles on either side of the transition, have been summarized in Table I for 13 dogs. Thus, each value entered in the On-Off or Off-On column represents the mean of 20 measured changes. The mean difference between the Off-On and On-Off transitions in 13 dogs was not large enough to be significant, and the 2 values were combined. The combined means, now based on 40 x 13 or 520 measurements for each hemodynamic parameter, show that use of the prosthetic myocardium increased aortic systolic pressure by 10.3% ± 3.9%, left ventricular pressure by 9.8% ± 4.8%, and cardiac output by 24% ± 10%. Left ventricular end-diastolic pressure was decreased by 16.5% ± 7.3%. Also shown are the weight of the dogs and the excised myocardium as percentage of free left ventricular wall weight. The excised myocardial tissue comprised, on the average, 26% of the free left ventricular wall.

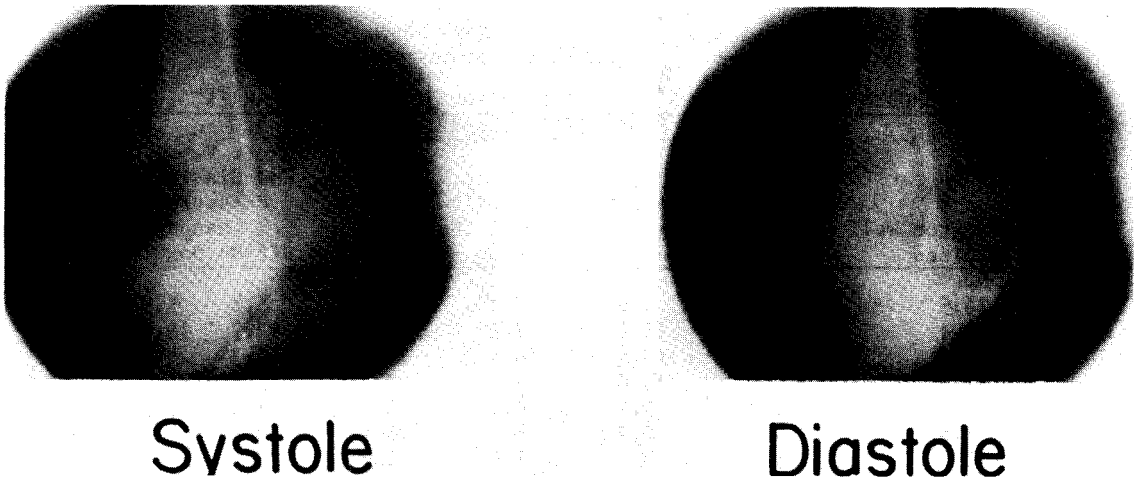

Figure 4. Ventriculogram with inactive prosthetic myocardium. Left - systole; right - diastole. Note limited reduction of ventricular volume during systole; predominant contraction is of the upper anterior wall.

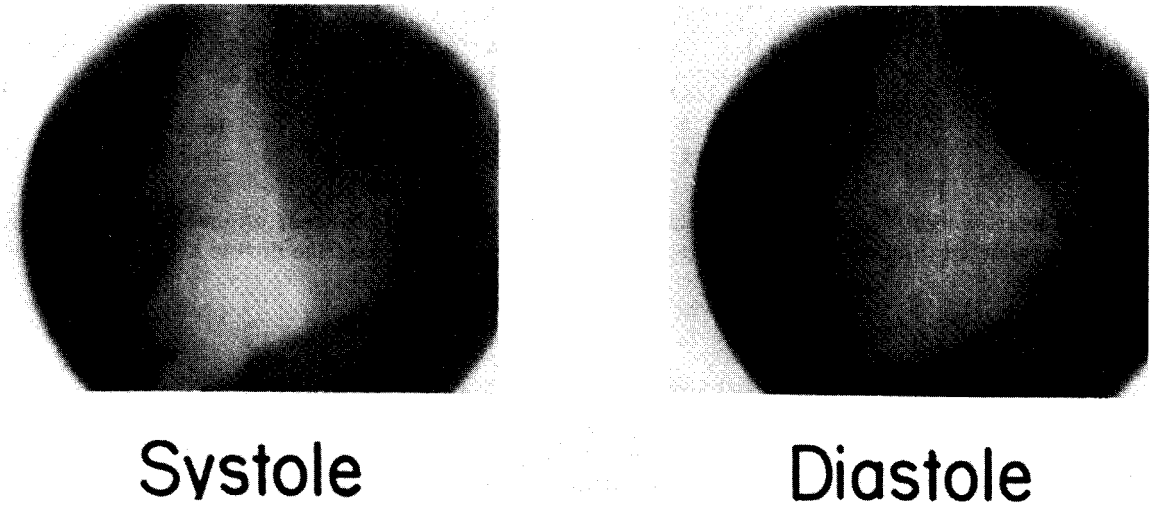

Figure 5. Ventriculogram with active prosthetic myocardium. Left - systole; right - diastole. Note appreciable reduction of ventricular volume resulting from contraction of the anterior, apical and lower posterior walls.

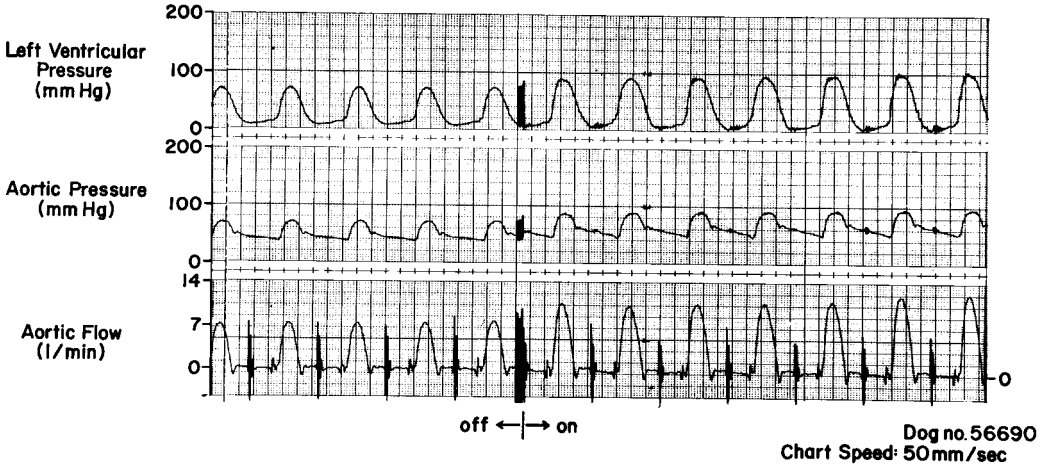

Figure 6. Hemodynamic response to activation of the prosthetic myocardium, showing increase in hemodynamic parameters after the device was turned on.

In 13 dogs, mean aortic systolic pressure increased from 76.2 ± 7.8 mm Hg to 84.1 ± 9.4 mm Hg, mean left ventricular systolic pressure increased from 75.5 ± 6.5 mm Hg to 83.0 ± 6.8 mm Hg, mean left ventricular end-diastolic pressure decreased from 8.5 ± 3.5 mm Hg to 7.1 ± 3.1 mm Hg, and mean cardiac output, normalized for B.W., increased from 32.1 ± 9.1 (ml/min/Kg) to 39.8 ± 12.5 (ml/min/Kg) (Figure 7). Figure 8 illustrates the transient response and shows myocardial adaptation to the activated prosthetic myocardium. Before activation, aortic pressure was 62 mm Hg, left ventricular systolic pressure was 62 mm Hg, left ventricular end-diastolic pressure was 12 mm Hg and cardiac output was 0.76 L/min. After activation, the hemodynamic parameters improved gradually. Four mins after continuous activation, aortic systolic and left ventricular systolic pressures had reached 86 mm Hg, left ventricular end-diastolic pressure had dropped to 8 mm Hg, and cardiac output had reached 1.6 L/min.

DISCUSSION AND CONCLUSION

Observations after excision of aneurysms and large infarcted areas have been reported by Danielson, et al[4]. These investigators produced myocardial infarction by ligation of coronary arteries and reported on a direct suture technique for repair of the ventricle after excision of the defect. They were able to obtain good results only when less than 13% of the left ventricle was excised. Collins and Collins[8] described a non-contractile prosthetic myocardium that replaced the excised part of the left ventricle. In their studies they observed that acute resection and replacement of left ventricular myocardium occurred at the expense of a reduction in cardiac output.

Schüpbach, et al[10] replaced an excised portion of the left ventricular wall with a prosthesis that acted by expanding into the left ventricle. The investigators demonstrated improved hemodynamic function during activation of the implant and established the feasibility of the concept. However, the device was effective only when implanted at the apex. In our study, a localized akinetic lesion was produced by removal of approximately 26% of the free left ventricular wall. This resulted in profound cardiogenic shock, defined as a state when systolic peak blood pressure dropped below 80 mm Hg. At the onset of activation, cardiac output quickly improved and continued to stay at a higher level as long as the prosthetic myocardium was activated. Systolic arterial pressure was likewise increased. The left ventricular end-diastolic pressure decreased immediately following assistance with the prosthetic myocardium.

The device described represents a promising step toward a method of replacing dysfunctional myocardium with a kinetic device. Further studies are necessary to investigate the details of tissue prosthesis interfaces, the attachment of the prosthesis to the myocardium, and the design of an implantable actuator and power source.

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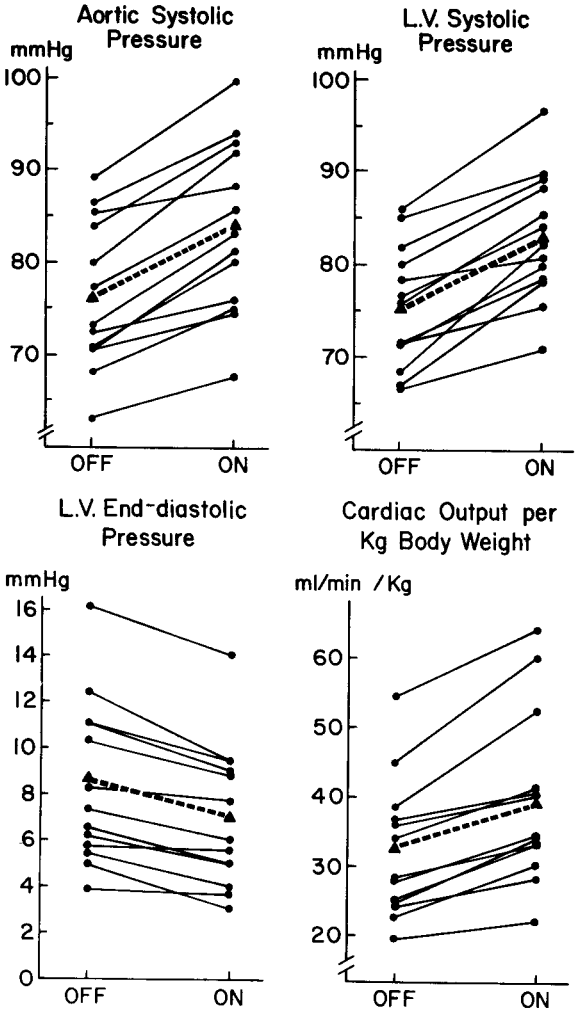

Figure 7. Effect of activation of the prosthetic myocardium on hemodynamic parameters in 13 dogs.

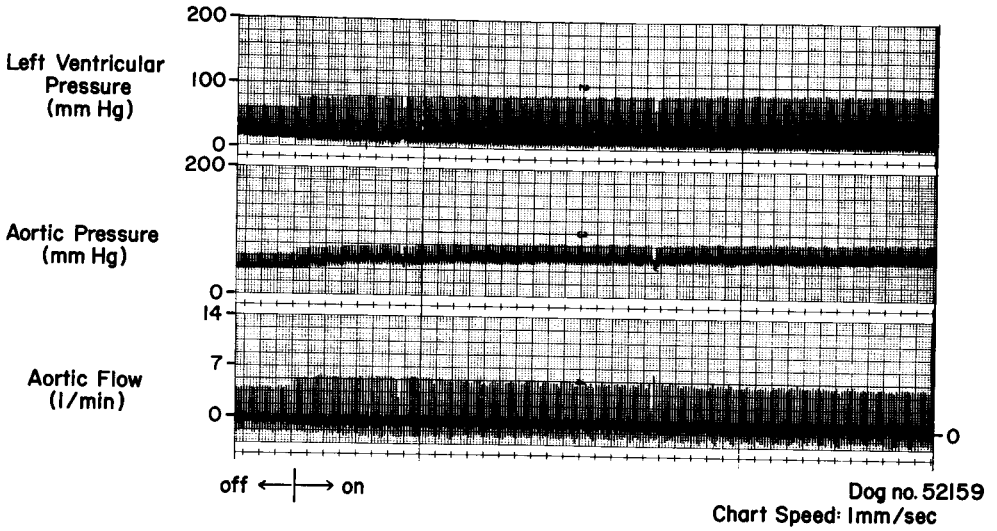

Figure 8. Transient response to activation of the prosthetic myocardium.